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# WILLIAM BULLOCH

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[*Obituary Notices of Fellows of the Royal Society 1941*]

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William Bulloch, Emeritus Professor of Bacteriology in the University of London and Consulting Bacteriologist to the London Hospital since his retirement in 1934, died on 11 February 1941, in his old hospital, following a small operation for which he had been admitted three days before. By his death a quite unique personality is lost to medicine, and to bacteriology an exponent whose work throughout the past fifty years in many fields, but particularly in the history of his subject, has gained for him wide repute.

Bulloch was born on 19 August 1868 in Aberdeen, being the younger son of John Bulloch (1837–1913) and his wife Mary Malcolm (1835–1899) in a family of two sons and two daughters. His brother, John Malcolm Bulloch, M.A., LL.D. (1867–1938), was a well-known journalist and literary critic in London, whose love for his adopted city and its hurry and scurry was equalled only by his passionate devotion to the city of his birth and its ancient university. On the family gravestone he is described as Critic, Poet, Historian, and indeed he was all three, for the main interest of his life outside his profession of literary critic was antiquarian, genealogical and historical research, while in his earlier days he was a facile and clever fashioner of verse and one of the founders of the ever popular *Scottish Students' Song Book.* He wrote authoritative histories of the University of Aberdeen and of its Lord Rectors, but genealogy was his dominating passion and the House of Gordon the chief object of his far-flung explorations. In a contribution to *Bon-Accord* (20 July 1929) on the Bulloch family in Aberdeen, he tells us that the grandfather, John Bulloch (1805–1882), a journeyman brassfounder, was born in Glasgow, and that the ancestral home of the Bullochs was the parish of Baldernock, a few miles north of that city. He adduces some evidence in support of the view that the Bullochs were originally Macdonalds from the Isles and descendants of a chieftain Donald, nicknamed 'Balloch', meaning 'freckled' in the Gaelic. In the same number of *Bon-Accord* is a note on the Bullochs of Georgia, a most aristocratic and influential Southern family who probably also trace their descent to the same Baldernock stock, and we are told that Dr Joseph Gaston Bulloch, the historian of the Bulloch family in America, visited the Aberdeen neighbourhood in the 'twenties in his search for relations.

John Bulloch the grandfather left the Clyde for Aberdeen in 1829 in response to an advertisement for brassfinishers, and from that date to 1922 Aberdeen was the family home. Though the residence link was then snapped by the death of their sister Lydia, a school teacher in Aberdeen, Malcolm says of himself, and to a lesser degree it could be said of his brother William who did not fully share Malcolm's *ingenium perfervidum Scotorum*, 'Though I have lived out of Aberdeen for six and thirty years, I am wholly in spirit a citizen of the never-to-be-forgotten Silver City by the sea with which I am in constant contact'.

The grandfather was a first-rate craftsman, and while Malcolm suggests that his brother William, who found his niche in science, inherited his grandfather's mechanical skill, there can be little doubt that both brothers owed their passion for bibliographic and genealogical enquiries to the grandfather's addiction to literary pursuits in his spare time, for his name will be found in the *Dictionary of National Biography* as the author of *Studies of the Text of Shakespeare* (London 1878) and other works, not to speak of a voluminous history of his relations which, says Malcolm, 'almost bewilders me by its wealth of detail'. The bookishness of the grandfather descended to his son, the father of Malcolm and William, who died in 1913. He was in early life an engraver, but later joined the commercial staff of the Broadford Works in Aberdeen, where he was employed for nearly fifty years and latterly as cashier until his retirement in 1906. In his leisure time the father edited *Scottish Notes and Queries*, and among his many contributions to antiquarian and historical research his *George Jamesone the Scottish Van Dyck* (Edinburgh 1885), who was born in Aberdeen, alleged to have studied under Rubens, and became a portrait painter in Aberdeen and later in Edinburgh, made its author widely known in influential literary circles. With such literary and book-loving forbears it is not surprising that William, like his brother Malcolm, turned to similar pursuits which more than competed with the attractions of their respective professional interests.

Bulloch and his brother were sent first to the Aberdeen Grammar School, but being there regarded as 'unsatisfactory pupils', or so William used to relate, they were transferred to the Old Aberdeen Grammar School, popularly known as 'The Barn'. From there the brothers proceeded in 1884 to King's College, and in due course Malcolm graduated M.A. in 1888, but two years of Arts subjects were enough for William, who went over in 1886 to medicine at Marischal College where he found himself. Though Bulloch had not shone as a student in Arts, there is no doubt that he picked up at King's much that stuck to him in later life, when some facility in the translation of classical medical texts became a stern necessity.

In 1890 he graduated M.B., C.M. with Highest Honours, receiving the John Murray Medal and Scholarship as the most distinguished graduate of the year. In the previous year he had won the Keith Gold Medal in systematic and clinical surgery. With a medical degree while not yet twenty-two, Bulloch doubtless found himself uncertain what to do next. For one year he acted as assistant to a doctor in practice, but the experience did not satisfy his soul, and having discovered in himself an urge towards research in pathology he returned to the university to work under Professor D. J. Hamilton in the Pathological Department. For a term of nine months in 1891 he served an apprenticeship in pathological histology, being attracted particularly by the pathology of the central nervous system. One result of his labours was a paper published in *Brain* in 1892 entitled

*Hyaline degeneration of the spinal cord.* The case investigated was one in which the nervous symptoms supervened after the patient had been suffering from ‘profound anaemia of the pernicious type’. Bulloch presented a very complete and well-illustrated study of the cord lesions, and in this, his first published paper, he shows himself familiar with the writings of his predecessors on the pathology of this uncommon condition, including those of French and German neuropathologists. No doubt the training under Hamilton whetted his appetite for wider experience, only to be had in these days in a German institute, but how was this to be managed? With a hundred pounds at his disposal, or so Professor Turnbull states, he proceeded in 1892 to Leipzig, where he spent a year in the Pathological Institute as a voluntary assistant under Birch-Hirschfeld, afterwards studying general medicine for a period of four months under distinguished masters at the Allgemeines Krankenhaus in Vienna. During his Leipzig days he was associated with Schmorl, who later went to Dresden, and with him he published a paper in 1894 on lesions of the lymph glands in diphtheria (*Lymphadenitis fibrosa*). On his return to Aberdeen he was again faced with a decision as to the next step, and on this occasion we are told that Arthur Keith, his senior by two years and already ensconced in London, persuaded Bulloch to try his fortune in the metropolis, so in 1894 we find him assisting Ferrier, a distinguished Arts graduate of Aberdeen, in the neuropathological laboratory at King’s College, afterwards receiving an appointment as assistant to Victor Horsley, Professor of Pathology at University College. Before Bulloch commenced his duties there, Horsley sent him to Paris to attend the course in bacteriology given by Roux and Metchnikoff at the Pasteur Institute, where he also attended the lectures of Duclaux. This experience definitely set Bulloch’s feet on the bacteriological ladder, and, little wonder, for these were the hey-days of the new science. Henceforth pathological anatomy and neurohistology in particular ceased to claim him as a wholehearted devotee, but the foundation of pathological knowledge he had laid was to serve him well in after years.

With Aldren Turner he carried out an enquiry in Ferrier's laboratory in 1894 on the histology of a case of bulbar paralysis, and the insight this gave him into methods of unravelling the central nuclei of cranial nerves must have served him in good stead in the preparation of his thesis for the Aberdeen M.D. entitled *The central connexions of the optic and ocular nerves in the higher mammalia.* For this thesis, presented in 1894, he was awarded Highest Honours and the Struthers Medal and Prize in Anatomy. The thesis has not, so far as I am aware, appeared in print.

In July 1895, owing to the resignation of Dr Bertram Hunt, who had officiated under Dr Armand Ruffer as Bacteriologist-in-Charge of the serum laboratories of the British Institute of Preventive Medicine since their establishment at Sudbury in December 1894, the vacancy so created was filled by the appointment of Bulloch who brought letters of recommendation from Horsley, Ferrier and D. J. Hamilton. The choice was a most fortunate one both for the young Institute and for Bulloch, for methods of serum production and methods of assay were then only very gradually being worked out, the latter chiefly at the hands of Ehrlich between whom and Bulloch there existed the friendliest relations. In this country the first horse to be immunized with diphtheria toxin had to be stalled at the Brown Institute during the summer of 1894 under the charge of Dr Armand Ruffer, the Acting Director of the British Institute of Preventive Medicine, and the removal of the serum production work to farm buildings and laboratories at Sudbury took place a few months later in December 1894. Sir Charles Sherrington has vivid memories of assisting Ruffer with the removal of blood from this first horse at the Brown and employing it with success in the treatment of a severe case of diphtheria. Bulloch's report to the Council in 1896 on his first year's work at Sudbury, where he had as assistants Dr St Clair Symmers (later of Cairo and Belfast) and Dr Harold Nolan (later of Cairo), registers progress in securing diphtheria antitoxin of fair potency for these early days. The serum so far produced had, we are told, a potency of 800–1000 'normal units' in 10 c.c., and Bulloch characteristically adds: 'Various samples of antidiphtheria serum in the market have been reported to contain 2–2½ times as many units in the same quantity of fluid, but the result of a very large number of experiments in testing the various serums has shown us that without exception they have fallen (in most cases considerably) short of their stated strength'.

Antistreptococcic serum and antitetanic serum were also being tentatively prepared and tested, while horses were being hopefully immunized with typhoid and cholera germs, staphylococci and pneumococci. In June 1897, after two years' work, Bulloch could report that the therapeutic dose of diphtheria antitoxin containing 1500 units could now be secured in a volume of 3 c.c., a very notable rise. Ehrlich had given Bulloch, as he continued to do to his successor Dr George Dean, every help in operating methods of assay which he had been working out and preparing for publication in his classic paper of 1897, *Die Werthbemessung des Diphtherieheilserums u. deren theoretische Grundlagen.*

There is no doubt that Bulloch found this almost virgin field of serum production and potency assay most stimulating and congenial, for through it he made lifelong friendships with leading investigators in the field, particularly Ehrlich, Salomonsen and Madsen. Lister, as chairman of the Council of the British Institute, took the keenest personal interest in the progress of Bulloch's work, for he had been greatly impressed by the report to the International Congress of Hygiene at Budapest in 1894 of Roux and Martin's experiences in the treatment of diphtheria by antitoxin. During Bulloch's service at Sudbury he was in 1896 appointed a member of a committee of the Royal College of Physicians and the Royal College of Surgeons to enquire into practical methods for the standardization of antitoxin, and doubtless, as Bulloch suggests in his application for the post of Bacteriologist to the London Hospital in 1897, the lion's share of the enquiry fell to him with the valuable first-hand experience he had acquired at Sudbury. Between 1896 and 1899 appeared four papers by Bulloch dealing with researches conducted at Sudbury and later prepared for publication. Two of these were devoted to *Streptococcus pyogenes* and antistreptococcic serum and two to diphtheria antitoxin. Like other similarly placed workers of the period Bulloch was stimulated by the success achieved with diphtheria antitoxin to enquire whether immunization of horses with other organisms such as *Streptococcus*, *Bacterium typhosum* and *Vibrio cholerae* might yield sera possessing similar properties. The remarkable variability we now know to exist within the streptococcal group was then not appreciated and consequently results then achieved with particular strains have interest and validity now only in so far as these particular strains are concerned. Bulloch took over horses whose immunization with streptococci was begun by Ruffer and continued with their immunization though hampered in his work by difficulties in maintaining virulence. After many months the sera yielded by the horses were found to possess only very mediocre therapeutic power. His account, however, of immunization experiments with two streptococcal strains, one from a case of erysipelas, and the other from an acute abscess, is of some interest as revealing the criteria employed by him in the attempt to discover to what extent an animal such as the horse would react to a particular strain after being immunized with another obtained from an entirely different source. The erysipelas strain could not be raised to the 'septicaemic' stage by repeated passage through the rabbit whereas the abscess strain was so raised in virulence by passage that one-millionth of a c.c. became a lethal dose. After nine months' immunization with the erysipelas strain the horse received 50 c.c. of the abscess strain with a M.L.D. for the rabbit of 0·0001 c.c. The result was a large swelling with no suppuration and Bulloch records as a remarkable finding that 'an animal immunized against a weak streptococcus is also to a very large extent immune to a streptococcus exalted to a highly septicaemic condition by passage through the rabbit'. By way of control he reports that a healthy horse which received only 0·05 c.c. of the abscess strain when its M.L.D. for the rabbit was 0·002 c.c. reacted only with a very large swelling and a temperature of 106° F. 'If', he writes, 'the two streptococci had been different in nature the immunized horse should have certainly succumbed to an injection of 50 c.c. of the abscess strain', and he therefore concludes that cross-immunity is attainable within the streptococcal group. As a brief contribution to the problem of the durability of passive immunity conferred by diphtheria antitoxin, then a much discussed question, Bulloch gave an ass 25,000 units of antitoxin subcutaneously and observed the fall in the antitoxin-content of the blood at intervals up to the 126th day. Assay by the Lo method, for the L+ was not then in vogue, showed that after 24 hours when the blood contained 16 units in 10 c.c. the titre fell progressively, but only after 126 days fell below one unit per 10 c.c. A calculation based on the assumption that the blood volume is one-thirteenth of the weight led him to postulate that the antitoxin introduced entered the blood for the most part and was not uniformly distributed throughout the body.

His contribution to the diphtheria toxin spectrum represents an effort on Bulloch's part to repeat in the case of two diphtheria filtrates Ehrlich's observations postulating the occurrence in such of atoxic or toxoid elements retaining the full combining power of toxin with antitoxin—a most important finding—together with other specific elements, proto-, deutero-, and syntoxoid and toxone. At this time Ehrlich's spectrum and his efforts to account quantitatively for all the antigenic equivalents satisfying one unit of antitoxin greatly intrigued workers engaged in serum standardization and for the most part confounded them. For many years now it has not been thought necessary to assume the presence of a variety of quotas of such bodies as Ehrlich postulated other than toxoid, and discussions of this subject on Ehrlich's lines are now of historical interest only. With Bulloch's departure from Sudbury his interest in these problems ceased.

*London Hospital Period (1897–1934)*.—Bulloch resigned his post at Sudbury on his appointment (27 June 1897) to the post of Bacteriologist to the London Hospital and Lecturer on Bacteriology and Pathological Chemistry to the London Hospital Medical School. He was then nearly twenty-nine years of age with a record of some eight years' experience in pathology, bacteriology and immunology both theoretical and practical which made him peculiarly fitted for this new sphere of activity. At the London he remained till his retirement in 1934 at the age of sixty-six. It was not, however, till 1919 that he received the title of Goldsmiths' Company Professor of Bacteriology (University of London) at the Medical College. This long connexion with the London did not cease with his retirement for he was at once appointed Consulting Bacteriologist to the hospital and Emeritus Professor in the University. It was not until war broke out that Bulloch ceased his daily visits to the hospital where he continued, as we shall see, his work in connexion with the bacteriological control of the London Hospital catgut and the many bacteriological problems associated with the manufacture of this substance. His application for the London Hospital post carried testimonials to his ability from many distinguished workers of the time both native and foreign, with all of whom he had been intimately associated. They included Lord Lister, Dr Allan Macfadyen, Professor G. Sims Woodhead, Professor Victor Horsley, Dr Émile Roux, Professor David Ferrier, Professor D. J. Hamilton his first teacher, Professor Birch-Hirschfeld, Dr Georg Schmorl, and last but not least, members of his first bacteriological class at University College which he had taught with such conspicuous success during the spring term of 1895.

Of his work at the London as teacher during these many years and of the influence on college and pupil that his precepts and personality exerted, others such as Professor H. M. Turnbull, Professor J. McIntosh and Dr Paul Fildes have written with high appreciation. My own intimacy with Bulloch as a director of research extended from September 1904 to September 1905, though as a student and graduate of his own school I had long before then been familiar with his name and repute. During this short year of pupillage, however, I had abundant opportunity of observing and confirming what these others have written of his methods of work and daily routine, of his personal influence and of the valuable precepts he inculcated to all and sundry for their guidance in research and never ceased to emphasize. He was, as Turnbull has written, 'a very hard and methodical worker', and he gloried in the fact that he could keep fit with little or no physical exercise, except on his annual holiday to the Cairngorms. All were impressed by his feats of memory and by his knowledge, derived from constant reading, of the beginnings and development of movements that seemed new to the tiro. Versed in bibliographic enquiry like his forbears he never failed to remonstrate with pupil or colleague when references in their papers for the press were slovenly or inaccurately recorded or possibly derived from some readily accessible second-hand source. 'Verify your references' was his invariable and salutary slogan, and pupils of his who have later trodden research paths certainly owe Bulloch much for the stimulus he gave them to careful survey of the beginnings of things touching their particular subject. Bulloch was indubitably right in emphasizing this aspect of research, for he felt strongly that to the younger generation of research workers the lack of a grounding in the history of their subject and of the contributions of its high priests was a serious handicap in assessing their own contributions or those of others.

The student listening to his first-hand tales of the works and ways of work, not forgetting the weaknesses, of the great teachers he had known, received impressions that were not likely soon to perish from the memory, even though they themselves might remain the 'fatheads' an exasperated Bulloch was often moved to call them. To the casual visitor or anxious enquirer in these early days Bulloch could be brusque and unbending if he scented pretence or suspected he was being put upon, and the notice on his private door, 'This is my busy day', was certainly not encouraging, but the brusqueness served only as a cloak of defence for at heart he was a straightforward, kindly and hospitable soul, eager to pass on the latest story from the mess table or to retell with embellishments in his inimitable style some piquant item from his vast store of *contes drolatiques*.

During the first ten or twelve years of his work at the London, Bulloch accomplished a considerable amount of original research on various themes, and his chief contributions to knowledge as distinct from his historical work belong in fact to this brief period. Even during this period, however, it became clear that he derived his one real interest and pleasure from his almost daily attendance after hospital hours in the medical libraries, where he could run down the beginnings and landmarks of a topical subject with scrupulous accuracy and surprising speed, so familiar was he with ways of getting rapidly down to work in libraries. Wide and continuous reading among the archives tended perhaps to inhibit what urge he had towards original and constructive investigation, or led him to abandon investigations when only half exploited. As Turnbull has said, 'Bulloch's knowledge of former good work tended to limit his laboratory research; he was apt to think that a subject had already been exhausted'. In the course of a lecture he gave at St Mary's Hospital in 1921 on the use and abuse of scientific medical literature, he makes the plea that a study of the work of others may afford a clue to the knowledge still required to elucidate some disease, and there is no doubt that he was justified in believing that much that deserves unearthing lies buried in the archives. Bulloch's reputation will in any case rest far more surely on his contributions to medical history and biography than on those to new knowledge based on experimental research. Fortunately during these first ten years of tenure of his London Hospital post Bulloch had with him a succession of seriously disposed voluntary workers and pupils with some of whom valuable co-operative work was accomplished. Of these I may mention J. J. R. Macleod, William Hunter (later of Hong-Kong), R. D. Keith (later of Singapore), P. Fildes, J. McIntosh, F. W. Twort, G. T. Western, E. E. Atkin, Major Greenwood, H. M. Turnbull and John Craw.

In 1900 Bulloch published a description of an exceedingly useful anaerobic jar in which anaerobiosis was secured by evacuation of air followed by replacement with hydrogen or coal gas and the subsequent removal of traces of oxygen by pyrogallic acid. For many years this very practical equipment has been in constant use in the laboratory either in its original form or in some modification, though recently jars based on more refined methods of getting rid of residual oxygen have come into use. In the catalogues the Bulloch jar still finds a place.

*Studies on haemolysis between 1900 and 1906.*—Bulloch evinced a keen interest in the fascinating new knowledge that was accumulating on the subject of haemolysis and the mechanics of action of antisera to foreign red cells, at the hands of Bordet, Ehrlich and Morgenroth, von Dungern and Madsen. With Hunter he published in 1900 a paper on a new bacterial haemolysin which they had for the first time demonstrated in three to four weeks' old cultures of *Bacillus pyocyaneus*. The paper is a thoroughly documented one and was communicated to the Pathological Society of London, but a full account of the work appeared also in the *Zentralblatt für Bakteriologie* in the same year. This haemolysin was capable of dissolving the red cells of various animals and appeared to be present only in the bodies of the bacilli from which it was released by autolysis. Some might be demonstrated in filtrates of old cultures, but filtrates of young cultures contained none of it. The pyocyanolysin was not found to be identical either with Emmerich and Low's pyocyanase or with the toxin demonstrable in broth filtrates which is pathogenic for certain laboratory animals. Some years later in 1906 as a contribution to *Studies in pathology* (a collection of papers by old pupils of D. J. Hamilton, edited by Bulloch on the occasion of the Quatercentenary of Aberdeen University, 1906), he placed on record studies on which he had been engaged for some years on the pathogenicity of *Bacillus pyocyaneus* and the possibility of acquiring immunity thereto. He, like others since, was unable to confirm the presence of a toxin (ectotoxin) in bacteria-free filtrates of this organism, as Wassermann alleged. On the other hand, guinea-pigs which are admittedly the experimental animals of choice for demonstration of pathogenic action by *Bacillus pyocyaneus* succumbed to whole broth cultures sterilized by toluol in doses of 0·5–1 c.c. Bacillary bodies washed off agar and killed with toluol were much less toxic and filtered autolysates of agar-grown bacilli had also little or no toxic effect on guinea-pigs or rabbits. It was only with difficulty that the virulence could be raised by passage, and the experience brought the remark that in respect of enhancement of virulence by passage, *Bacillus pyocyaneus* differed fundamentally from *Streptococcus* and *Pneumococcus.* Immunization failed to induce any high degree of immunity. Since these days the immunology of this interesting organism seems to have received but little attention, and the precise nature of such immunity as may be secured by immunization is still uncertain.

In 1903 Bulloch made an early contribution to the question of inhibition of lysis of red cells by certain salts, even in isotonic concentration, in the presence of immune body and complement. He showed, for example, that when the corpuscles were suspended in isotonic solution of magnesium sulphate, the minimum haemolytic dose of the amboceptor which in physiological saline was only 0·0007 c.c. had to be raised to 2 c.c. The inhibition of the lysis in such cases he satisfied himself to be due not to destruction of complement but to prevention by the salt of the union of complement with immune body. The magnesium sulphate did not prevent the sensitization of the red corpuscle by the amboceptor.

Attracted by Ehrlich's work on the mechanism of the transmission of immunity from parents to offspring and naturally interested as he was in the phenomena of inheritance, Bulloch communicated to the Pathological Society of London in 1902 a brief note of results of mating experiments with rabbits either normal or immunized with foreign red cells. He found no evidence of haemolysin in the offspring of a highly immunized father if the mother was normal. If the mother was immunized after conception, abortion was frequent, but the foetal fluids contained abundant lysin. If the mother was immunized before conception, any difference in the haemolytic titre of serum of mother and offspring was due simply to varying complement.

When the two sera were inactivated and complemented there was little or no difference between the titres.

Like Ehrlich whose observations he, in the main, confirmed, he believed that the mother's milk was the most important vehicle of transference of immune bodies after birth, though technical difficulties were encountered in estimating such bodies with accuracy in a milk medium. Unfortunately his experiments, designed to determine whether the offspring from normal or non-immunized parents would acquire lysin in its blood by sucking an immunized foster-mother, failed owing to reluctance of the latter to take kindly to the progeny of others. One point noted by Bulloch in connexion with this work and which deserves notice was the long persistence of demonstrable lysin in the blood serum after the conclusion of the primary immunization course.

*The nature and mode of action of the 'opsonin' of Wright and Douglas.*—During the years 1905 and 1906 Bulloch communicated two papers on this subject to the Royal Society in collaboration respectively with E. E. Atkin and G. T. Western. The experiments, as far as they went, were interpreted by the writers as demonstrating that the opsonin in normal serum was, as Wright believed, not identifiable with any hitherto described antibody and was of relatively simple constitution. Moreover, they concluded from digestion experiments with different organisms that the normal opsonin possessed a considerable degree of specificity. Controversy on these points, in which the writer shared, cannot be said to have entirely ceased now, but space precludes detailed criticism of the conclusions reached by Bulloch in his contribution to this problem in the light of the vast literature which has accumulated on the mode of action of similarly functioning antibodies in normal and immune sera. The account by Robert Muir of this perplexing subject in the *System of Bacteriology*, which is full and detailed, may be consulted.

During my sojourn in Bulloch's department in 1904 he published with me an experimental study of the behaviour of opsonin in serum following the injection of leucocytosis-producing substances. This study revealed the fact that an early and considerable rise of opsonin but of short duration occurred only when the substance employed was a nucleinate derived from yeast and probably contained some readily absorbable antigenic quota. When other chemical substances with greater powers of inducing leucocytosis than nuclein were employed, no rise of opsonin occurred. A further study of this remarkable effect of nuclein together with attempts to unravel its mechanism was later made by Bedson in 1914. Incidentally the reduced phagocytic power of the newly formed polymorphonuclear leucocytes thrown into the circulation was placed on record. Bulloch's interest in the nature of the opsonic substance during those early years was the prelude to his entering with enthusiasm the field of vaccine therapy and its assessment by measurements of the opsonic index. As consultant to the King Edward VII Sanatorium he was naturally interested in the behaviour of the opsonic index in tuberculous patients in comparison with normals, and in the influence on this index of tuberculin, X-rays, and Finsen light, etc. Later, his enthusiasm cooled considerably, and, if we may judge from addresses and reviews on this subject, he became correspondingly sceptical of securing unbiased proof of the efficacy of vaccine therapy. If one reads his amusing contribution in 1910 to the discussion on vaccine therapy at the Royal Society of Medicine, in which he pokes fun at the empiricism of clinicians and their habit of drawing conclusions from clinical impressions only, one gathers that he himself despaired of securing data free from bias and amenable to statistical analysis. The position has not greatly altered even now. This contribution by Bulloch shows him at his best in the rôle of critic of the clinician and his ways—a rôle he heartily relished without exhibiting the least vindictiveness.

Apart from these more sustained enquiries on haemolysis and opsonic action, Bulloch and his collaborators have to their credit individual scientific contributions to a variety of subjects, some of which deserve notice. In collaboration with J. J. R. Macleod an early study of the chemical constitution of the tubercle bacillus appeared in 1904, in which an effort was made to track down the element to which acid-fastness was due. With Sequeira, in 1905, he published in what has been justly regarded by pathologists as a classical paper, observations on the relation of the suprarenals to the sexual organs in the light of certain cases that had come to their notice in young children of sexual precocity associated with the presence of tumours derived for the most part from the adrenal cortex. Bulloch had made an extensive hunt in the literature for similar cases, and he and Sequeira deserve great credit for drawing the attention of the medical profession to a new syndrome which since that time has become widely known and widely studied. To Bulloch also with his collaborators John Craw and E. E. Atkin must be given the credit of demonstrating in three papers in 1906, 1908 and 1909 the imperfections of certain widely used kieselguhr filters in holding back bacteria and for revealing by stringent tests the underlying causes. Complaints by manufacturers of the incriminated filters led only to renewed experiments which completely confirmed the previous work.

I have said that Bulloch's experimental work in the laboratory was accomplished practically entirely during the first ten or twelve years of his working life. Between 1909 and 1934 when he retired from his post at the London, the only important piece of experimental work with a very definite practical bearing was his study of catgut, the bacteriological control of which had been for a number of years in Bulloch's charge. The fruits of his experimental work together with a masterly historical survey of catgut and other binding substances employed in surgery appeared as a green book in the *Medical Research Council Special Report Series* in 1929, and in it were included experimental data on physical and physico-chemical problems connected therewith by Lampitt and Bushill of the Research Laboratories of Messrs J. Lyons & Co. This co-operation in a field of cardinal importance to surgery was brought about by Mr Alfred Salmon, head of the firm of Messrs J. Lyons & Co. and a member of the House Committee of the London Hospital for many years. Bulloch's contribution to the green book runs to 121 pages and deals in succession with the historical development of catgut in surgery, the anatomy of the sheep's intestine, the preparation of the gut, the action of a variety of disinfectants, and the controls to be observed in the testing of catgut for bacteriological sterility. On this last point he laid the greatest emphasis in view of his own findings that many of the then commonly used disinfectants such as biniodide of mercury, carbolic acid, and corrosive sublimate acted only as temporary bacteriostatics. Accurate testing for sterility demanded the removal by appropriate chemicals of the deposited salts when it was generally discovered that the material was far from sterile. Bulloch found that 1 per cent aqueous iodine was the disinfectant of choice because of its penetrating powers and its ability to sterilize outright. One disadvantage, however, was that the tensile strength was to some extent interfered with by prolonged immersion in iodine, and this physical aspect of the problem is discussed in Lampitt and Bushill's contribution. The catgut green book will long remain a hunting-ground and source of reference to all who may in future be concerned with the perfecting of catgut for surgical and other uses.

*Bibliographic and historical work.*—It can truly be said that from the date of his first published paper in 1892 Bulloch never failed in all his subsequent work to acquaint himself and his less curious readers with practically all the really important studies on any subject to which his attention was directed. The hunt itself thrilled him, and often he had the satisfaction of exposing the weaknesses of others less concerned than he was with the securing of accuracy by reference to the originals. His passion for bibliography led to his services being enlisted by compilers of systems of medicine, etc., demanding authoritative treatment of their various chapters. These efforts by Bulloch in a variety of fields have a permanent value, and it may be taken for granted that references to, and descriptions of, originals by Bulloch represent the fruit of his own independent consultation. His first effort in this field on the pathological anatomy of acquired syphilis of the nervous system appeared in 1899 in Albutt's *System*, and it was quickly followed by careful reviews on haemolysis (1901), cytotoxins (1901), tuberculosis and tubercle bacilli (1902), rheumatic fever (1906), psorospermosis (1907), bacteriotherapeutics (1907) and plague (1907). That he was able to engage in this bibliographic work amid his laboratory and teaching preoccupations during this early period of his career is assuredly testimony to his industry and determination to make the most of the shining hour. His contributions to the *Treasury of human inheritance*, edited by Pearson of the Francis Galton Laboratory for National Eugenics during the years 1909–10, including that on haemophilia prepared with the assistance of Paul Fildes, demand special notice, not only for their intrinsic merit and permanent value, but also for their revelation in Bulloch himself of what, as I have already said, was truly a family addiction to genealogical pursuits. In the lecture to which I have alluded on the use and abuse of scientific medical literature he described his own efforts to trace real authority for certain statements about haemophilia which he often found to rest on second-hand or hearsay evidence. Out of hundreds of papers consulted by himself and Fildes on the subject of haemophilia only a small handful were presented with the completeness necessary for valid inference. Intervening in the course of a debate on heredity at the Royal Society of Medicine on 2 December 1908, when Karl Pearson was defending his methods against a persistent critic who favoured the Mendelian School, Bulloch remarked that he knew very little about Mendelism or Pearsonism, but he had been engaged for a number of years in collecting pedigrees which had been published of human diseases and he believed he had as complete a collection as had ever been brought together.

Thus spoke one who undoubtedly deserves to be regarded as a pioneer in the securing of basal data for the scientific study of human genetics.

To the *Orth-Festschrift* in 1903 Bulloch contributed a paper on the teaching of pathology in Great Britain and in the metropolitan medical schools, in the course of which he commented on the serious lack, except in Scotland, of regular professorships of pathology in the teaching universities. Later, in 1906, as a contribution to *Studies in Pathology*, he gave a most interesting account of the history and progress of the Sir Erasmus Wilson Chair of Pathology at Aberdeen and of D. J. Hamilton, its first occupant. Among Hamilton's pupils who contributed original articles to this volume were St Clair Symmers, W. Leslie Mackenzie, A. R. Cushny, George Dean, Alexander Low, William Hunter. J. J. R. Macleod, G. F. Petrie, R. D. Keith, W. Bulloch (who edited the volume), J. C. G. Ledingham and Arthur Keith. When I went to work with Bulloch in 1904 as a Carnegie Fellow, I was promptly nicknamed Carnegie, and to Bulloch I remained so to the end. It was only much later that I discovered in Bulloch's references to the needs of universities in his history of Hamilton's Chair that Carnegie subsidies to Scottish students did not have his full approval. 'Let money be sought', he writes, 'for equipment of laboratories, encouragement of research, and the endowment of our libraries.'

*The history of bacteriology* (*1938*).—For many years Bulloch had been making first-hand acquaintance with original works in all languages bearing on the various concepts that have been held of such phenomena as contagion, fermentation, putrefaction, infection, etc., culminating in the discoveries of Pasteur which heralded the bacteriological era. These researches must have involved an enormous amount of wide and intensive reading, and their value is considerably enhanced by the pains he took to investigate the personal histories and careers of many of the leading lights in his galaxy of pioneers. To the *System of Bacteriology* he contributed not only an article on the History of Bacteriology in the first volume (1930) but also notes on landmarks in the development of our knowledge of all the important pathogens discussed in this treatise. In 1937 he delivered the Heath Clark lectures before the University of London, and Bulloch's masterpiece, *The History of Bacteriology*, published in 1938, was ostensibly based on these lectures. I say 'ostensibly' but the history really embodies the fruits of a lifetime's addiction to bibliographic pursuits undertaken with the definite objective of unveiling the beginnings and evolution of a new science. The appearance of Bulloch's book has, it may be noted, given a great fillip to historical studies in the bacteriological field, especially in America where its advent was heartily welcomed, and there is now perhaps little excuse for the still prevailing ignorance among budding research workers in bacteriology of the history and the personalities of its great past.

The writing of obituaries and of descriptive accounts of the careers of many of these personalities was to Bulloch almost a sacred charge, and these obituaries are mines of information. Spallanzani was a particular hero of his, and we are told he studied Italian seriously in his later years, the better to follow the work and wanderings of his hero with a view to a complete biography of this versatile scientist.

A congratulatory address from the Lister Institute to the University of Pavia on the occasion of the Spallanzani celebration in April 1939 was written by Bulloch as Chairman of the Governing Body in language which clearly reveals him as Spallanzani's devoted admirer. In the course of it he writes: 'It is probably true to say that no student of nature of any age has approached the Abbate Spallanzani in the immense range of his work or in the accuracy of his conclusions. During his lifetime his fame was recognized everywhere and since his death it has grown. He is now universally included in that small band of investigators whose researches will live for ages.'

Mr Clifford Dobell, who for many years was in closest touch with Bulloch and who shared to the full the latter's interest in historical research, informs me that he hopes to be able after the war to edit and publish Bulloch's manuscripts and notes on Spallanzani which are now in his possession.

The following obituaries by Bulloch appeared in various journals including the *Proceedings of the Royal Society*, in the years as bracketed below: Emanuel Klein (1925), Charles Creighton (1927), Alexander Ogston (1929), W. M. W. Haffkine

(1931), Baron Kitasato (1931), Sir William Watson Cheyne (1932), Martinus Willem Beijerinck (1932), Émile Roux (1933) and Theobald Smith (1935). He also wrote on special features of the achievements of Spallanzani (1922), of Pasteur (1922), of Robert Koch (1932) and of Lord Lister (1927), the last in connexion with the centenary of Lister's birth celebrated in that year.

*Roll of Fellows of the Royal Society.*—For a number of years before his death Bulloch had been engaged in compiling a biographical record of Fellows of the Society from the very commencement of the Society's foundation. Mr Dobell informs me that the roll was left in manuscript with no directions as to its disposal. It is gratifying now to learn that it has been acquired by the Society and will be published as soon as feasible after the war. In Dobell's view it is a monumental work and 'will probably be regarded in years to come as one of his chief contributions to learning'. Sir Charles Sherrington writes me with regard to this roll: 'Through a number of years Bulloch devoted time and labour and industrious care to the collection of the widely scattered biographical material relating to past Fellows of the Royal Society. Starting with the first list of 1663 he brought his material down to quite recent years, but the names and careers of some of them were hard to trace biographically. I am told that he had succeeded so well that finally the number of Fellows whom he could not so trace amounted only to three or four. A difficulty encountered by his self-imposed task centred round the early years of the Society's roll. For certain names of these years the lapse of time has made it difficult to secure a personal history. Bulloch devoted to his enquiry a zest and patience which never flagged. He ransacked libraries, turned over archives and he looked through old academical lists of universities from Oxford and Edinburgh to Leyden and Montpellier. The dealers in seventeenth and eighteenth century books knew him. He wrote to namesakes of the old names, and sometimes proceeded to an interview involving a long journey. He used to speak smilingly of the refractory residuum of past Fellows who in spite of all his efforts still remained from his point of view 'lifeless' ghosts. It was a privilege to me to assist him at the final unearthing and resurrection of one such. For instance, a small eighteenth century book on chemistry catalogued by the second-hand bookseller as by Robert Boyle led to a dénouement of a satisfying kind. The volume stated itself to be by 'F. R. S.' but otherwise it was anonymous. Bound into it after the 'Finis' was a page list of other printings from the same Press. This list was less discreet as to authorship, and from it with a little ingenuity the name of the anonymous F. R. S. was discoverable. It proved to be that of a ghost whom Bulloch had been enquiring after for many years. In consequence the Society's library now contains a little series of his works. His name was William Aglionby and he is no longer ghostly. Bulloch thus compiled a biographical catalogue of the Fellowship which will be of high value to a future historian of the Society and he has the Society's gratitude for so doing.'

*Bulloch's activities on committees.*—A mere list of the expert committees on which Bulloch served and whose published reports he helped to compile must suffice. His services on these committees were of great value particularly perhaps in securing, as he alone could, an accurate historical background for any apparently novel movements or technical processes that might be discussed.

*Antityphoid Inoculation Committee.*—Inaugurated May 1904. The interim report of this committee appeared in 1906 along with a minority report signed by Bulloch and A. E. Wright who retired from the Committee. The disagreement was over what at the time was regarded as a very trivial point. *Medical Research Committee, Special Advisory Committee upon bacteriological studies of cerebrospinal fever during the epidemic of 1915.* This reported in 1916. *Medical Research Committee, Special Committee upon the standardization of pathological methods:* Three reports of this committee appeared in green book form in 1918 and one in 1920. *Medical Research Committee, Committee upon anaerobic bacteria and infections:* Of this committee Bulloch was chairman and its report appeared in 1919. In 1923 appeared a substantial volume entitled *Diphtheria: its bacteriology, pathology, and immunology*, the chapters of which were written but not individually signed by members of the Bacteriological Committee of the Medical Research Council. Many meetings took place at which the contributions and views of each member were subjected to the severest and frankest criticism prior to acceptance. The first chapter on the history of diphtheria was, as may readily be imagined, written by Bulloch, and a masterly account it is, involving the most extensive researches by him into the original sources. Up to quite recent years also, Bulloch served on the Foot-and-Mouth Disease Research Committee of the Ministry of Agriculture.

In these special Committees Bulloch could at times supply trenchant and valuable criticism, but as a rule he was content to take only a small part in actual discussions which of necessity were often highly controversial. His attitude to these might be described as pacifist, reflecting on his part a reluctance to commit himself. Nevertheless he missed nothing and forgot nothing of what went on, and seemed to derive a real satisfaction from the contemplation of the more warring spirits among his colleagues.

In addition to membership of expert committees Bulloch held at various times other honourable administrative offices. He was an original member of the Medical Research Committee (later the Medical Research Council) and served thereon from 1914 to 1921. He was a member of the Executive Committee of the Imperial Cancer Research Fund and of the Scientific Advisory Committee of the Beit Memorial Trust from its foundation. He held the office of President of the Pathological Section of the Royal Society of Medicine in 1917, and from 1925 to 1935 he acted as its Honorary Librarian, becoming an Honorary Fellow of the Society in 1940. In 1910 he delivered the Horace Dobell Lecture before the Royal College of Physicians on *Problems of pulmonary tuberculosis considered from the standpoint of infection*, and was Tyndall Lecturer at the Royal Institution in 1922, when he dealt with spontaneous generation, heterogenesis, etc., in the light of Tyndall's work and that of Spallanzani and Pasteur. He was also an honorary member of the Pathological Society of Great Britain and Ireland, and he had acted as an examiner for the Universities of London, Leeds and Liverpool and the Royal College of Veterinary Surgeons. His experiences as an examiner yielded him a fund of humorous tales of absurd and desperate replies by examinees which he retailed with great gusto for years afterwards in many an after-dinner speech. In 1913 he was elected F.R.S., and in 1920 his old university conferred upon him the honorary degree of LL.D. In 1918 he was elected a member of the Governing Body of the Lister Institute on whose staff he had served from 1895 to 1897, and from 1932 he was its chairman, having succeeded Sir David Bruce in this capacity. In the affairs of the Lister Institute Bulloch always maintained a keen interest, and as chairman of its Governing Body he greatly enjoyed the task of summarizing the year's research work for the Members of the Institute at their Annual Meeting. For some years before his retirement from the London in 1934 Bulloch was showing signs of incipient paralysis agitans which, however, progressed only very slowly and did not greatly impede his work and outside activities. In fact it was not until a few months before his death that the disease led to a serious deterioration of his condition. The last meeting of the Governing Body which he attended took place on 29 November 1940, but after that date I had letters from him on Lister business written in his beautiful handwriting and with his favourite violet ink.

As I have said, he entered the London Hospital on 8 February and he died on 11 February after a rapid suprapubic cystostomy.

In his will the University of Aberdeen and the Lister Institute appear as residuary legatees.

In 1923 Bulloch had married Irene Adelaide, widow of Alfred Augustus Baker. She survives him with a stepdaughter, Monica, now Mrs Clifford Dobell.

*Acknowledgements.*—In the preparation of this obituary I have had the valuable help of Clifford Dobell, F.R.S., whose bibliography of Bulloch's writings follows. For various items of

information I am indebted to Sir Charles Sherrington and to three Aberdeen friends, John Smith, M.D., F.R.C.P., George Duncan, C.B.E., LL.D., and J. F. Tocher, D.Sc., LL.D.

To all these I would express my sincere thanks.

J. C. G. LEDINGHAM

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No complete list of William Bulloch's publications has yet been printed, and its compilation is a formidable task: for he wrote much, in many different places, over a period of close on half a century; and although he delighted in tracking down and cataloguing the works of others, he never made any adequate attempt to assemble his own. From a bibliographical standpoint, the few relevant notes and papers which he has left are, indeed, almost worthless—even misleading. He did not even keep copies of some of his own chief writings.

Consequently, the following bibliography cannot claim to be complete. It has been collected, without his aid, under great difficulties and limitations imposed by the present war—with London's libraries bombed-out or evacuated, and many obvious sources of information rendered temporarily inaccessible. A proper bibliography will only be possible with the return of peace and leisure. Nevertheless, the following list is full—if not complete. It contains every notable publication which I have been able to trace; and I have checked every entry by personal examination of the originals in order to attain the maximum of accuracy in details. A few notes are added [in square brackets] where they appear desirable.

In addition to the publications here specifically cited, Bulloch wrote innumerable abstracts, reviews or summaries of other authors' works. These appeared in various medical and scientific journals, and occasionally even in the popular press—seldom signed, sometimes initialled, more often anonymously. All—so far as they are known to me—have been excluded intentionally. The principle adopted has been to include every publication—however trivial—of which he was author, part author or joint author (these distinctions are carefully noted), but only in so far as it contains material information or data contributed by himself. The attribution of initialled articles is from personal knowledge of their authorship: I have accepted nothing at second hand—following his own precept and practice, which were in the best tradition.

Although all his abstracts have been excluded, it should be noted that Bulloch contributed a large number to the *Medical Supplement to the Daily Review of the Foreign Press* (compiled by the Medical Research Committee and issued by the War Office), volumes I–II, 1918–19; and also to its sequel *Medical Science* (issued by the Medical Research Council), volumes I–XII, 1919–25. For the sections on bacteriology and pathology in both these periodicals he was editorially responsible, and he spent much time and labour in their preparation. From 1911 onwards he also acted, with Sir Leonard Hill, as general editor of Messrs Edward Arnold's *International Medical Monographs*, though he contributed nothing to this series in his own name.

Bulloch's two fine Tyndall Lectures at the Royal Institution (1922) were never published, and no manuscript now appears to exist. They were delivered on May 16 and 23, and entitled 'Tyndall's Biological Researches' and 'The Foundations of Bacteriology'. The substance of these lectures was incorporated later in his *History of Bacteriology* (1938).

Appreciative notices of Bulloch himself appeared in 1934, on the occasion of his enforced retirement from active life (see especially *Lond. Hosp. Gaz.* **38**, 2, and *Vet. Rec.* **14** (n.s.), 822—both articles accompanied by portraits). Noteworthy obituaries have since been published by *The Times* (13. ii. 41—which erroneously states that 'he worked with Robert Koch in Germany'); and in *Lancet* (1941), **1**, 263 (by P. F[ildes]—with early portrait); *Brit. Med. J.* (1941), **1**, 341 (by H. M. T[urnbull]—with same portrait); *Lond. Hosp. Gaz.* (1941), **44**, 95 (by H. M. T[urnbull] and others—with same portrait as in 1934); *Nature* (1941), **147**, 504 (by J. McIntosh); *Aberdeen Grammar School Mag.* (1941), **44**, 127 (including a tribute by A. Keith—with the portrait here reproduced); *J. Path. Bact.* (1941), **53**, 297 (by P. F[ildes]—with same portrait as in *Vet. Rec.* 1934); *Aberdeen Univ. Rev.* (1941), **28**, 119 (by G. Duncan and L. Hill); and *Vet. J.* (1941), **97**, 86 (by J. McC[unn]—with another portrait).

I cannot conclude this note without a personal tribute. For over twenty years William Bulloch was one of my best friends and wisest counsellors, and my marriage to his wife's daughter towards the end of this period consolidated our friendship and familiarity. I can therefore say—as he said of Lister—that 'I had the great privilege of knowing him in a manner which, considering the disparity of our positions, was almost intimate'. I might even say that it was intimate: and his death is thus, to me, literally an irreparable loss. He was a friendly and informal man of extraordinary intellectual energy and astonishing erudition, with uncommon knowledge of the world and of men and women generally—upright in his own life and habits, downright in his judgements and opinions of others, and withal a most lovable, generous, sincere and trustworthy person in every way. As Hamlet said of his father (and Bulloch was one of my own spiritual fathers, besides being legally my stepfather-in-law):

> He was a man, take him for all in all,
> I shall not look upon his like again.

But he has left his own monuments to Science, and his reputation and individual qualities will undoubtedly shine with even greater lustre in the years to come. The Royal Society has already gained much from his devoted labours in our interest, and it stands to gain still more in future—when his *Roll of the Fellows* is made public. Meanwhile, I can do no more than follow in his footsteps (*longo intervallo*) by attempting to chronicle his yet published works in a manner conformable with his own noble example and ideals.

Clifford Dobell

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